Outcome after simultaneous PCI and left atrial appendage occlusion

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Summary

Aims: To investigate feasibility and safety of concomitant percutaneous coronary intervention (PCI) and left atrial appendage occlusion (LAAO) as compared to PCI in combination with antithrombotic treatment in patients with coronary artery disease and nonvalvular atrial fibrillation (AF).

Methods and results: Patients with AF undergoing concomitant PCI with drug-eluting stents (DES) and LAAO with dedicated devices were consecutively entered into a prospective single-centre registry and were compared to AF patients from the Bern DES registry treated with different antithrombotic strategies. Among 379 patients with AF, 56 patients were treated with concomitant PCI and LAAO, 268 patients were treated with PCI and dual therapy (DT), and 55 patients were started on triple antithrombotic therapy (TT). Clinical follow-up was assessed by standardised telephone interviews. Patients with PCI + LAAO were older (76 ± 7 years) as compared to patients with PCI + DT (72 ± 9 years) or PCI + TT (73 ± 8 years) (p <0.01). They more commonly had a history of cerebrovascular events (31% vs 10% vs 16%, p <0.001). CHA_2DS_2-vasc scores amounted to 3.5 ± 2.2, 3.6 ± 1.3, and 4.2 ± 1.3 among patients with PCI + LAAO, PCI + DT, and PCI + TT, respectively (p = 0.03). At 30 days, the composite of all-cause death, myocardial infarction, ischemic stroke, or BARC bleeding type 3–5 was documented in 12.5% of patients undergoing PCI + LAAO, 8.2% in patients with PCI + DT, and 9.2% in patients with PCI + TT, with no significant differences between groups in an age-adjusted analysis (PCI + DT being the reference; PCI + LAAO: HR 1.27 (95% CI 0.54–2.99), p = 0.58; PCI + TT (1.19 [95% CI 0.49–2.92], p = 0.70). Two patients (3.6%) with PCI + LAAO suffered a periprocedural stroke, and 5 patients (8.9%) were recorded to have bleeding BARC type 3a or 3b. At 1 year, all-cause mortality in patients with PCI + DT, amounted to, 6.7% (reference). It was 6.3% (HR 0.51, 95%CI 0.12–2.20, p = 0.36) and 18.2% (HR 2.89, 95% CI 1.33–6.26, p <0.01) in PCI + LAAO and PCI + TT, respectively. There was no difference with regards to the composite of all-cause death, myocardial infarction, ischaemic stroke, or bleeding (BARC type 3–5) (PCI + DT being the reference; PCI + LAAO: HR 1.17 (95% CI 0.56–2.45), p = 0.67; PCI + TT (1.68 [95% CI 0.89–3.15], p = 0.11).

Conclusion: PCI with concomitant LAAO is a feasible alternative to combined anti-platelet and anti-thrombotic management in patients with CAD and AF. Longer-term follow-up will be needed to demonstrate efficacy.

Key words: left atrial appendage occlusion; atrial fibrillation; coronary heart disease; percutaneous coronary intervention; antiplatelet therapy; anticoagulation; drug-eluting stents

Background

Atrial fibrillation (AF) coincides with coronary artery disease (CAD) given common risk factors and pathophysiologic pathways. CAD affects approximately every fourth AF patient according to the trial Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM), while in the Global Registry of Acute Coronary Events (GRACE) atrial fibrillation affected about 9% of patients with CAD [1–3]. The optimal medical regimen in these patients remains a matter of debate. This is particularly true for patients undergoing percutaneous coronary intervention (PCI) and require antiplatelet therapy. We reported the prevalence of AF in patients undergoing percutaneous coronary intervention (PCI) to be approximately 5% [4]. Combination of vitamin K antagonists (VKA) with antiplatelet treatment imposes an additional risk of bleeding. Finding a safe and effective balance between the risk of ischaemic events and bleeding complications is challenged by shared risk factors for either event such as advanced age, hypertension, or renal disease. Triple antithrombotic therapy with acetylsalicylic acid, clopidogrel, and VKA has been associated with a considerable risk of bleeding events in patients with myocardial infarction and stable coronary artery disease [4, 5]. Dual therapy with clopidogrel and VKA has been documented to offer favourable safety and efficacy outcomes as compared to triple therapy [6, 7].

Percutaneous left atrial appendage occlusion (LAAO) is a proven alternative to oral anticoagulation in patients with nonvalvular AF [8, 9]. With longer follow-up in the randomised PROTECT-AF trial, LAAO showed superiority over VKA with regard to cardiovascular death and a trend towards better stroke prevention [10]. In a high-risk population, such as AF-patients undergoing PCI, LAAO may be an attractive treatment option by obviating the need for combined oral anticoagulation and antiplatelet therapy.

The objective of the present analysis was therefore to

investigate clinical outcome of patients with CAD undergoing PCI and nonvalvular AF according to treatment with dual-antiplatelet therapy in combination with LAAO (PCI + LAAO), dual therapy (PCI + DT), or triple therapy (PCI + TT).

Methods

Patient Population

All patients with nonvalvular AF and CAD leading to PCI with DES were prospectively entered into a database at Bern University Hospital, Switzerland, between April 2002 and March 2009. Patients with AF and CAD undergoing PCI and LAAO with dedicated devices were enrolled in a prospective clinical registry started in 2009. Written informed consent was obtained from all patients. Both registries have been approved by the Ethics Committee at Bern University Hospital, Switzerland, and complied with the Declaration of Helsinki.

Procedures

PCI procedure

PCI was performed in accordance with current standards of care. A femoral access was chosen in all patients. In some patients undergoing elective PCI, VKA was discontinued 3 days prior to the procedure in order to achieve an International Normalised Ratio (INR) <2.0. In particular, patients presenting with acute coronary syndromes underwent PCI without a VKA-free interval and regardless of INR measurement. During the procedure, all patients were loaded with acetylsalicylic acid 250–500 mg and unfractionated heparin in a dose of 70–100 IU/kg or at least 5000 IU. The consecutive antiplatelet and anticoagulation therapy was installed upon the discretion of the operator. After the procedure a control electrocardiogram was performed in all patients and creatine kinase (CK), CK-MB, and troponin T were assessed to determine peak enzyme levels.

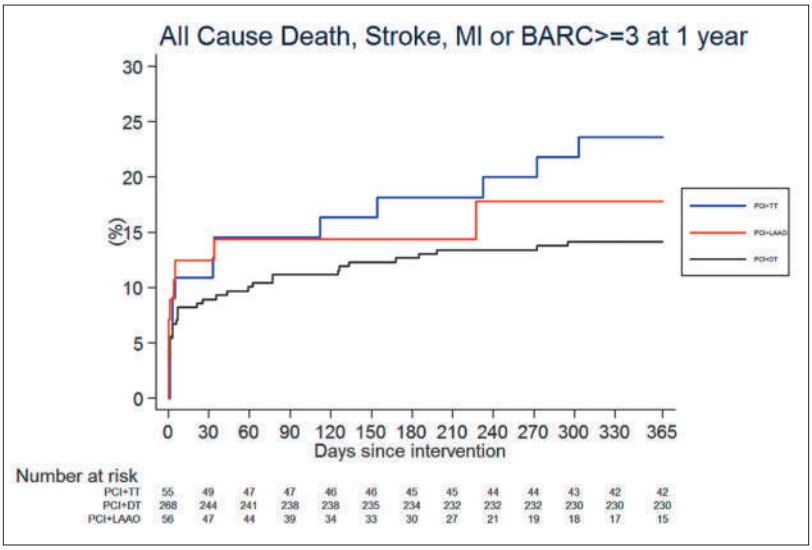

Figure 1: Events per treatment strategy. BARC = bleeding academic research consortium; MI = myocardial infarction.

Left atrial appendage occlusion

In patients receiving both PCI and LAAO within the same session, PCI was usually performed prior to LAAO. A transoesophageal echocardiogram (TOE) was performed prior to the procedure to rule out thrombus formation in the LAA, except for patients undergoing ad-hoc LAAO where thrombus in the left atrial appendage was excluded by contrast injection to the left atrium [9]. All procedures were performed under local anaesthesia with fluoroscopic guidance only (no TOE). The Amplatzer Cardiac Plug (ACP, St. Jude Medical, Plymouth, MN, USA) was used in all patients. The left atrium was accessed either by a transseptal puncture or by a patent foramen ovale (PFO) or atrial septal defect (ASD) if such was present (in which case the defect was closed using an Amplatzer PFO or ASD Occluder through the same delivery sheath at the termination of the procedure). The LAA was sized by contrast medium injections through the 13 French Amplatzer TorqVue delivery sheath (St. Jude Medical, Plymouth, MN, USA) in at least 2 projections. The outer diameter of the sheath (5.5 mm) served as reference for sizing. The aim was to oversize the device by at least 20%. After deploying the device a stable position was confirmed by a tug test and contrast medium injection.

After the procedure and before hospital discharge, a control transthoracic echocardiogram was performed to document a stable position of the device. Oral anticoagulation was stopped immediately after implantation in most cases and antiplatelet therapy was installed according to the discretion of the operator.

Data collection

Follow-up was performed by standardised telephone interviews. In patients treated with LAAO, a control TOE was performed after 3–6 months to exclude device thrombus and residual leaks and to confirm proper sealing of the LAA. In case of a potential adverse event, hospital record documentations from primary care physicians and referring cardiologists were collected. All cardiac and bleeding events were adjudicated by cardiologists and all neurologic events by neurologists. All data were entered into a dedicated database.

Definitions

AF was defined as at least 1 documented episode of irregularly irregular rhythm of at least 30 seconds duration. We did not differentiate between intermittent, persistent, or permanent AF for the purpose of this analysis. Triple therapy was defined as the combination of acetylsalicylic acid, clopidogrel, and VKA. Dual therapy was defined as VKA in combination with acetylsalicylic acid or clopidogrel or the combination of two platelet inhibitors. Cardiac death was defined as death resulting from cardiac reasons, procedure-related mortality, or death of unknown cause. Myocardial infarction (MI) encompassed Q-wave and non-Q-wave MI and was documented with the presence of new pathological Q-waves in ≥2 contiguous leads or elevation of CK to ≥2 × upper limit of normal (ULN) and a rise in CK-MB or troponin to ≥3 × ULN. Neurologic events were classified into transient ischaemic attack (TIA), ischaemic stroke, or unclear neurologic events. Transient ischaemic attack was defined as a focal neurologic deficit that resolved completely within 24 hours and showed no signs of ischaemia in computed tomography or magnetic resonance imaging. Ischaemic stroke was defined as a focal neurologic deficit persisting for >24 hours or with the evidence of a corresponding ischaemic lesion in an imaging examination. A neurologic event was classified as unclear when patients reported neurologic symptoms but there was no documentation which would allow further classification into stroke or TIA. Bleeding events were adjudicated according to the definitions provided by the bleeding academic research consortium (BARC) [11].

Statistical analysis

Baseline characteristics of patients were first depicted for 3 groups according to the treatment they received concomitantly with PCI. Discrete data were summarised as counts and frequencies (%) with p-values from Chi-Square, whereas continuous data were presented as means ± SD with p-values from ANOVAs. Counts of clinical outcomes and their incidence rates from Kaplan-Meier life tables were then displayed. Cox regressions were performed to compute hazard ratios of clinical outcomes at 30 days and 1-year follow-up, PCI + DT being the reference group. Adjustment was done for age as well as for other baseline characteristics (age, gender, CHA_2DS_2-vasc score, and left ventricular ejection fraction). Two-sided p-values less than 0.05 were considered as statistically significant. All analyses were performed using Stata version 13.0.

Results

A total of 379 patients with AF and CAD undergoing PCI were included into the present analysis. Of them, 56 patients with AF deemed at increased risk of bleeding were treated with concomitant PCI + LAAO and no further VKA, 268 patients were treated with dual therapy (DT; 195 [73%] with double antiplatelet treatment, and 73 [27%] with VKA and single antiplatelet therapy) and 55 patients were treated with VKA, acetylsalicylic acid, and clopidogrel (TT). Baseline characteristics are summarised in table 1. Patients treated with PCI + LAAO were older than patients treated with PCI + DT or PCI + TT (76 ± 7 versus 72 ± 9 versus 73

Table 1: Baseline characteristics.

Baseline characteristics	PCI + LAAO	PCI + DT	PCI + TT	p-value
N = 379	N = 56	N = 268	N = 55	
Age years (SD)	76.4 ± 7.2	72.0 ± 9.1	73.1 ± 8.1	0.003
Sex, male n (%)	14 (25.0%)	68 (25.4%)	18 (32.7%)	0.513
BMI mean kg/m² (SD)	27.7 ± 4.6	27.0 ± 4.5	28.7 ± 5.4	0.086
Cardiovascular risk factors				
Hypertension n (%)	52 (92.9%)	171 (63.8%)	42 (76.4%)	<0.001
Diabetes mellitus n (%)	18 (32.1%)	52 (19.4%)	16 (29.1%)	0.055
Clinical features				
Renal failure (creatinine ≥200 µmol/l) n (%)	7 (12.7%)	4 (1.7%)	1 (2.0%)	<0.001
Congestive heart failure	9 (21.4%)	110 (41.0%)	26 (47.3%)	0.025
Prior stroke or TIA	13 (31.0%)	26 (9.7%)	9 (16.4%)	0.001
LV ejection fraction mean (SD)	54.3 ± 11.7	50.7 ± 12.6	48.4 ± 14.3	0.082
CHA_2DS_2	2.9 ± 1.3	1.9 ± 1.2	2.3 ± 1.2	<0.001
CHA_2DS_2-vasc score	3.5 ± 2.2	3.6 ± 1.3	4.2 ± 1.3	0.030

Depicted are means ± SD with p-values from ANOVAs, or counts (%) with p-values from chi-square tests.
BMI = Body-Mass-Index; LV = left ventricle; TIA = transient ischaemic attack.

Table 2: Clinical outcome.

Clinical Outcome	All patients N = 379	PCI+LAAO N = 56	PCI+DT N = 268	PCI+TT N = 55
30-day follow-up				
Death n (%)	12 (3.2)	0 (0.0)	7 (2.6)	5 (9.1)
Cardiac events				
Cardiac death n (%)	9 (2.4)	0 (0.0)	5 (1.9)	4 (7.4)
Myocardial infarction (MI) n (%)	10 (2.7)	0 (0.0)	10 (3.7)	0 (0.0)
– Q-wave MI n (%)	5 (1.3)	0 (0.0)	5 (1.9)	0 (0.0)
– Non Q-wave MI n (%)	5 (1.3)	0 (0.0)	5 (1.9)	0 (0.0)
Neurologic events				
Ischaemic stroke	4 (1.1)	2 (3.6)	2 (0.7)	0 (0.0)
TIA	1 (0.3)	0 (0.0)	1 (0.4)	0 (0.0)
Unclear neurologic event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bleeding Events				
BARC 3a	12 (3.2)	4 (7.1)	6 (2.2)	2 (3.6)
BARC 3b	4 (1.1)	1 (1.8)	3 (1.1)	0 (0.0)
BARC 3c	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
BARC 4	1 (0.3)	0 (0.0)	1 (0.4)	0 (0.0)
BARC 5a	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
BARC 5b	2 (0.5)	0 (0.0)	1 (0.4)	1 (1.9)
Composite Outcomes				
Death / MI / ischaemic stroke	24 (6.3)	2 (3.6)	17 (6.3)	5 (9.1)
Cardiac death / MI / ischaemic stroke	21 (5.6)	2 (3.6)	15 (5.6)	4 (7.4)
Death / MI / ischaemic stroke / BARC bleeding 3–5	37 (9.8)	7 (12.5)	24 (9.0)	6 (10.9)
Cardiac death / MI/ ischaemic stroke/ BARC bleeding 3–5	34 (9.0)	7 (12.5)	22 (8.2)	5 (9.2)
1-year follow-up				
Death n (%)	30(8.2)	2 (6.3)	18 (6.7)	10 (18.2)
Cardiac events				
Cardiac death n (%)	17 (4.7)	1 (1.9)	9 (3.4)	7 (13.0)
Myocardial infarction (MI) n (%)	13 (3.5)	1 (3.4)	11 (4.1)	1 (2.0)
– Q-wave MI n (%)	5 (1.3)	0 (0.0)	5 (1.9)	0 (0.0)
– Non Q-wave MI n (%)	8 (2.2)	1 (3.4)	6 (2.3)	1 (2.0)
Neurologic events				
Ischaemic stroke	7 (1.9)	2 (3.6)	5 (1.9)	0 (0.0)
TIA	1 (0.3)	0 (0.0)	1 (0.4)	0 (0.0)
Unclear neurologic event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bleeding Events				
BARC 3a	13 (3.5)	4 (7.1)	7 (2.6)	2 (3.6)
BARC 3b	6 (1.6)	1 (1.8)	4 (1.5)	1 (2.0)
BARC 3c	1 (0.3)	0 (0.0)	1 (0.4)	0 (0.0)
BARC 4	1 (0.3)	0 (0.0)	1 (0.4)	0 (0.0)
BARC 5a	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
BARC 5b	2 (0.5)	0 (0.0)	1 (0.4)	1 (1.9)
Composite outcomes				
Death / MI / ischaemic stroke	46 (12.5)	5 (8.9)	30 (11.2)	11 (20.0)
Cardiac death / MI / ischaemic stroke	35(9.5)	4 (7.1)	23 (8.6)	8 (14.9)
Death / MI / Ischaemic stroke / BARC bleeding 3–5	60 (16.1)	9 (16.1)	38 (14.2)	13 (23.6)
Cardiac death / MI / ischaemic stroke / BARC bleeding 3–5	50 (13.5)	9 (16.1)	31 (11.6)	10 (18.5)

Depicted are counts (incidence rates % from Kaplan Meier life tables).
BARC = bleeding academic research consortium; MI = myocardial infarction; TIA = transient ischaemic attack

Table 3: Age adjusted clinical outcome.

Cox regression with reference group as PCI + DT	Age-adjusted analysis			
	PCI + LAAO		PCI + TT	
	HR (95%CI)	p-value	HR (95%CI)	p-value
30-day follow-up				
Death	n.e		3.81 (1.20–12.12)	0.023
Cardiac death	n.e		4.05 (1.08–15.14)	0.037
Myocardial infarction	n.e		n.e.	
Ischaemic stroke or TIA	2.86 (0.46–17.94)	0.262	n.e.	
Ischaemic stroke or MI	089 (0.19–4.11)	0.878	n.e.	
BARC bleeding ≥3	1.92 (0.66–5.61)	0.234	1.31 (0.37–4.70)	0.678
Death / MI / ischaemic stroke	0.48 (0.11–2.12)	0.336	1.40 (0.52–3.80	0.507
Cardiac death / MI / ischaemic stroke	0.59 (0.13–2.63)	0.493	1.28 (0.42–3.85)	0.664
Death / MI / ischaemic stroke / BARC bleeding 3–5	1.27 (0.54–2.99)	0.578	1.19 (0.49–2.92)	0.697
Cardiac death / MI / ischaemic stroke / BARC bleeding 3–5	1.45 (0.61–3.45)	0.397	1.16 (0.44–3.07)	0.761
1-year follow-up				
Death n (%)	0.51 80.12–2.209	0.363	2.89 (1.33–6.26)	0.007
Cardiac death n (%)	0.49 (0.06–3.91)	0.499	3.98 (1.48–10.70)	0.006
Myocardial infarction n (%)	0.50 (0.06–4.00)	0.518	0.46 (0.06–3.55)	0.454
Ischaemic stroke or TIA	1.58 (0.31–8.10)	0.584	n.e.	
Ischaemic stroke or MI	1.09 (0.31–3.86)	0.894	0.33 (0.04–2.50)	0.283
BARC bleeding ≥3	1.48 (0.53–4.16)	0.455	1.39 (0.46–4.23)	0.559
Death / MI / ischaemic stroke	0.84 (0.32–2.18)	0.714	1.80 (0.90–3.60)	0.095
Cardiac death / MI / ischaemic stroke	0.88 (0.30–2.60)	0.824	1.70 (0.76–3.81)	0.194
Death / MI / ischaemic stroke / BARC bleeding 3–5	1.17 (0.56–2.45)	0.671	1.68 (0.89–3.15)	0.107
Cardiac death / MI / ischaemic stroke / BARC bleeding 3–5	1.43 (0.67–3.05)	0.349	1.72 (0.84–3.50)	0.138

HR are from Cox regression.

± 8 years; p = 0.003), respectively, and more commonly had a history of previous stroke (31% versus 10% versus 16%; p = 0.001).

Clinical outcomes at 30 days and at 1 year are shown in table 2. At 30 days, the composite of all-cause death, myocardial infarction, ischaemic stroke, or bleeding type 3–5 according to the BARC definition was documented in 12.5% of patients undergoing PCI + LAAO, 8.2% in patients with PCI + DT, and 9.2% in patients with PCI + TT, with no significant differences between groups in an age-adjusted analysis (PCI + DT being the reference; PCI + LAAO: HR 1.27 (95%CI 0.54–2.99), p = 0.58; PCI and TT (1.19 [95%CI 0.49–2.92], p = 0.70) (table 3). Two patients (3.6%) with PCI and LAAO suffered a periprocedural stroke. One patient developed acute somnolence, hypotension, and hemiplegia during the intervention. A cerebral angiography showed no occlusion of major cerebral arteries. Symptoms resolved almost completely within 24 hours; however, at discharge the patient had a residual mild paresis of the left hand. The second patient developed a complete hemiplegia, hemineglect, and aphasia the night after the intervention. A CT-scan showed a subacute ischaemic insult. On the second postinterventional day the patient had a residual mild paresis of the hand a central facial nerve paresis, and a gaze paresis. Symptoms improved spontaneously until discharge. Five patients (8.9%) were recorded as having bleeding BARC type 3a or 3b. At 1 year, the rate of cardiac death amounted to 1.9%, 3.4%, and 13.0% in patients with PCI + LAAO, PCI + DT and PCI + TT, respectively. The composite of all-cause death, MI, ischaemic stroke, and BARC bleeding type 3–5 was documented in 17.8% of patients with PCI + LAAO, 14.2% of patients with PCI+DT, and 23.6% of patients with PCI + TT. No new bleeding or neurologic events were documented in the group of patients treated with PCI + LAAO between 30 days and 1 year.

LAAO and TT were compared with DT in an analysis adjusted for age only (table 3) and for all differences in baseline characteristics (table 4). There were no significant differences with respect to all individual and composite endpoints.

Discussion

The key findings can be summarised as follows. (1.) Patients with AF and CAD are at high risk of major adverse cardiac, cerebrovascular, or bleeding events through 1 year of follow-up; (2.) PCI with concomitant

Table 4: Baseline variables adjusted clinical outcome.

Cox regression with reference group as PCI + DT	Baseline characteristics-adjusted analysis*			
	PCI + LAAO		PCI + TT	
	HR (95%CI)	p-value	HR (95%CI)	p-value
30-day follow-up				
Death	n.e		4.47 (1.31–15.26)	0.017
Cardiac death	n.e		4.93 (1.24–19.69)	0.024
Myocardial infarction	n.e		n.e.	
Ischaemic stroke or TIA	1.71 (0.21–14.11)	0.621	n.e.	
Ischaemic stroke or MI	0.89 (0.18–4.27)	0.883	n.e.	
BARC bleeding ≥3	2.12 (0.71–6.30)	0.178	1.21 (0.33–4.37)	0.772
Death / MI / ischaemic stroke	0.55 (0.12–2.42)	0.427	1.30 (0.47–3.54)	0.614
Cardiac death / MI / ischaemic stroke	0.65 (0.14–2.90)	0.571	1.18 (0.39–3.59)	0.770
Death / MI / ischaemic stroke / BARC bleeding 3–5	1.44 (0.61–3.42)	0.404	1.10 (0.45–2.70)	0.840
Cardiac death / MI / ischaemic stroke / BARC bleeding 3–5	1.61 (0.67–3.86)	0.3285	1.00 (0.38–2.66)	0.995
1-year follow-up				
Death n (%)	0.52 (0.11–2.37)	0.399	2.93 (1.33–6.45)	0.008
Cardiac death n (%)	0.40 (0.05–3.53)	0.409	4.33 (1.57–11.95)	0.005
Myocardial infarction n (%)	0.54 (0.07–4.28)	0.556	0.43 (0.05–3.34)	0.417
Ischaemic stroke or TIA	1.33 (0.22–7.98)	0.754	n.e.	
Ischaemic stroke or MI	1.17 (0.33–4.22)	0.806	0.29 (0.04–2.19)	0.228
BARC bleeding ≥3	1.52 (0.53–4.39)	0.435	1.35 (0.44–4.14)	0.600
Death / MI / ischaemic stroke	0.96 (0.37–2.54)	0.941	1.68 (0.83–3.37)	0.147
Cardiac death / MI / ischaemic stroke	0.99 (0.33–2.92)	0.979	1.60 (0.71–3.60)	0.258
Death / MI / ischaemic stroke / BARC bleeding 3–5	1.32 (0.63–2.79)	0.460	1.57 (0.83–2.97)	0.164
Cardiac death / MI / ischaemic stroke / BARC bleeding 3–5	1.57 (0.73–3.37)	0.250	1.49 (0.73–3.06)	0.274

HR are from Cox regression.
*The baseline adjusted models control for age, gender, CHA_2DS_2-vasc score and left ventricular ejection fraction at baseline. BARC = bleeding academy research consortium; MI = myocardial infarction; TIA = transient ischaemic attack

LAAO is a feasible alternative to combined antithrombotic and antiplatelet therapy and adding the risk of an additional and technically demanding procedure to PCI did not result in a higher complication rate; (3.) larger studies with randomised design will be needed to assess safety and efficacy of combined LAAO and PCI as compared to conventional treatment.

Our study has several limitations. First, we present a historical comparison of patients treated with combined antiplatelet and antithrombotic therapy between 2002 and 2009 and LAAO between 2009 and 2013. The recent introduction of non-VKA oral anticoagulants (NOAC) has led to a paradigm shift in in the treatment of nonvalvular AF and has introduced a competitive comparator. However, the combination of NOAC with antiplatelet agents is not recommended by current guidelines preventing this treatment strategy as an approved comparator at this time. Second, the non-randomised treatment allocation to PCI + LAAO, PCI + DT or PCI + TT introduces a selection bias. Due to small numbers of patients, we could not perform a propensity score matched analysis. Nonetheless we adjusted the analysis for differences in baseline characteristics to address the non-randomised treatment allocation. However, differences between groups may be underestimated by latent factors. Third, we included a small number of patients with only a short duration of follow-up into this analysis. Efficacy of LAAO is expected to have a growing advantage over chronic oral anticoagulation during long-term follow-up when bleeding complications in PCI + DT and PCI + TT patients more than outweigh the front-loaded procedural complications in PCI + LAAO patients.

Studies investigating optimal treatment strategies for AF and CAD address the 2 entities isolated from each other, thus neglecting the frequent combination of the 2 diseases. The subset of patients with AF and CAD is exposed to an increased risk of ischaemic and haemorrhagic events and has an increased risk of death as compared to patients with either one of the conditions. This is not only explained by the addition of the individual risk of both disease entities, but may also result from a collateral effect of colliding treatment strategies. Aggressive antithrombotic

treatment with TT has been shown to increase the risk of bleeding complications as compared to VKA and acetylsalicylic acid or clopidogrel [5, 7]. The combination of clopidogrel and VKA appeared to offer the best balance between benefit and risk.

LAAO has proven effective in patients with AF to the end to further reduce the risk of bleeding in this patient population. Successful device implantation was achieved in all patients in our analysis. However, we documented a considerable rate of periprocedural bleeding in patients with LAAO amounting to 9% which was slightly higher than previous reports. Procedures were performed in consecutive, unselected patients (reflecting a real world setting which is often associated with higher event rates as compared to randomised controlled trials), were combined with PCI procedures, and also reflect our ear LAAO experience with Amplatzer devices. This puts our results into proper perspective. As LAAO is a challenging intervention, there may be a rather shallow learning curve hampering the clinical outcome of this initial series. Besides a relatively high rate of periprocedural bleeding events, we observed two peri-interventional strokes (4%). In turn, no new ischaemic or haemorrhagic events were documented in the group of patients treated with PCI and LAAO between 1 month and 1 year. In view of the limited number of patients this may be a chance finding. On the other hand it may also indicate efficacy of LAAO for the prevention of adverse events in this patient population, consistent with previous findings in patients with isolated AF.

In conclusion, we present an initial series of patients treated simultaneously with PCI and LAAO and show the feasibility of the concept. Larger studies with randomised design will be required to assess safety and efficacy of this approach as compared to medical treatment.

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DK and TP share first authorship/equal contribution.

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